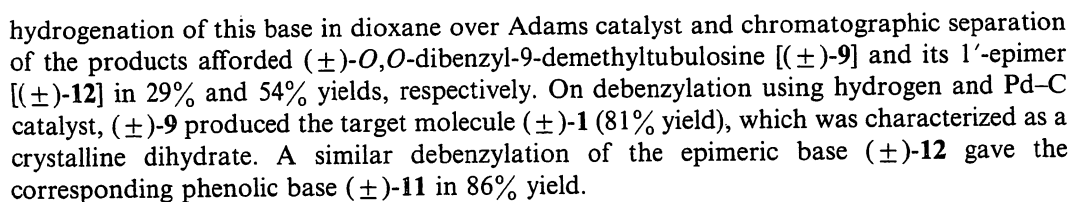


Quinolizidines. XIV. A racemic synthesis of 9-demethyltubulosine, an alkaloid isolated from *Alangium vitiense*

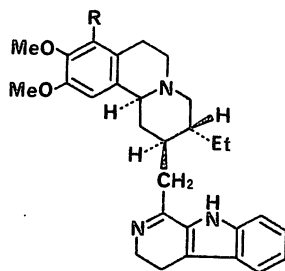
著者	Ohba Masashi, Hayashi Mitsuko, Fujii Tozo
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The key intermediate generated in our synthetic plan was the racemic tricyclic amino acid (\pm)-7, which was prepared in eight steps from the *trans*-lactam ester (\pm)-5 *via* the lactim ether (\pm)-6 according to the previously reported procedure.¹⁰⁾ Condensation of (\pm)-7 with 5-benzyloxytryptamine in *N,N*-dimethylformamide (DMF) by the diethyl phosphorocyanidate method¹¹⁾ gave the amide (\pm)-8 in 93% yield. The amide (\pm)-8 was then cyclized with POCl₃ in boiling toluene to furnish the dihydro- β -carboline (\pm)-10 in 69% yield. Catalytic

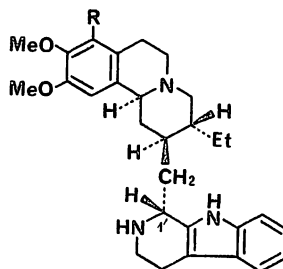


The assignments of the configuration at C-1' of (\pm)-**1**, (\pm)-**9**, (\pm)-**11**, and (\pm)-**12** were based on four criteria, namely, the ratio of the two C-1' isomers formed, thin-layer

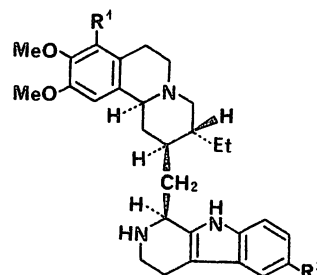
chromatographic (TLC) mobility, and ^{13}C nuclear magnetic resonance (^{13}C -NMR) and ^1H -NMR spectral features. As regards the first criterion, the formation of a 1 : 1.9 mixture of (\pm)-**9** and (\pm)-**12** in the above catalytic reduction of (\pm)-**10** is comparable to that¹²⁾ of a 1 : 2 mixture of deoxytubulosine (**15**) and isodeoxytubulosine (**18**) or to that¹⁾ of a 1 : 1.9 mixture of *O*-benzylalangimarckine (**16**) and the $1'\alpha$ -H isomer (\pm)-**20** in the analogous reduction of the dihydro- β -carboline **13** or **14**. As regards the second criterion, the TLC mobilities of (\pm)-**1** and (\pm)-**9** were found to be greater than those of their $1'$ -epimers (\pm)-**11** and (\pm)-**12**, respectively. This chromatographic behavior corresponds to that observed for the analogous $1'$ -epimeric pairs tubulosine (**3**)-isotubulosine (**19**),¹³⁾ emetine (**26**)-isoemetine (**27**),¹⁾ **16**-**20**,¹⁾ and alangimarckine (**17**)-**21**.¹⁾



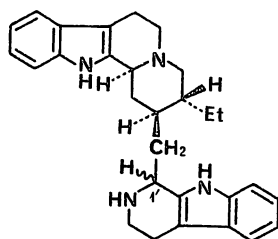
13 : R = H
14 : R = OCH₂Ph



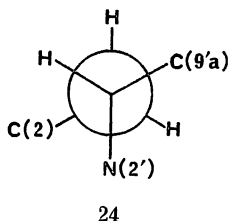
15 : R = H
16 : R = OCH₂Ph
17 : R = OH



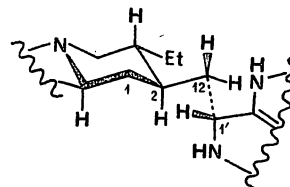
18 : R¹ = R² = H
19 : R¹ = H; R² = OH
20 : R¹ = OCH₂Ph; R² = H
21 : R¹ = OH; R² = H



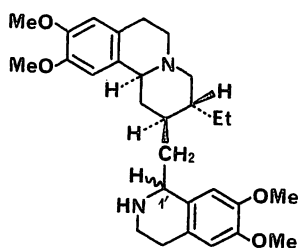
22 : $1'\beta$ -H
23 : $1'\alpha$ -H



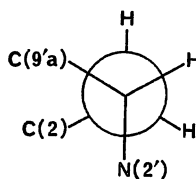
24



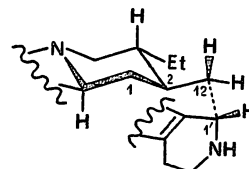
25



26 : $1'\beta$ -H
27 : $1'\alpha$ -H



28



29

As regards the third criterion (^{13}C -NMR), it may be seen from Table I that the C(1), C(2), and C(1') carbon signals of (\pm)-**9** appeared upfield from the corresponding signals of the $1'$ -epimer (\pm)-**12** by 1.4–2.9 ppm, whereas the differences in chemical shift between the other corresponding carbons of the two isomers were insignificant. A similar feature has been found by Koch *et al.*¹⁴⁾ for ochrolifuanine A (**22**) and ochrolifuanine B (**23**), and they

proposed a preferred conformation, as represented by the partial structure **25**, for the 1' β -H isomer **22**. We have observed the same trends for the isomeric pair emetine (**26**)–isoemetine (**27**) and utilized them successfully for differentiating alangimarckine (**17**) from its 1'-epimer (**21**).¹¹ The ¹³C-NMR spectral features of (\pm)-**1** in Me₂SO-*d*₆ (Table I) also indicated the 1' β -H configuration to be correct for this phenolic base.

The fourth criterion employed for the stereochemical assignment was the ¹H-NMR spectral features, as shown in Table II and in the experimental section. It may be seen that the C(10)-methoxy protons of (\pm)-**12** and (\pm)-**11** resonated at higher field than did those of (\pm)-**9** and (\pm)-**1** by 0.29 and 0.22 ppm, respectively. Such a relationship has been found by

TABLE I. ¹³C-NMR Data for (\pm)-9-Demethyltubulosine (**1**), (\pm)-*O,O*-Dibenzyl-9-demethyltubulosine (**9**), and the 1' α -H Isomer (\pm)-**12**

Carbon ^{b)}	Chemical shift ^{a)}			Carbon ^{b)}	Chemical shift ^{a)}		
	(\pm)- 1 ^{c)}	(\pm)- 9 ^{d)}	(\pm)- 12 ^{d)}		(\pm)- 1 ^{c)}	(\pm)- 9 ^{d)}	(\pm)- 12 ^{d)}
C(1)	36.5	36.9	38.3 ⁱ⁾	C(4')	22.4	22.8	22.8
C(2)	35.9	36.5	37.9	C(4'a)	106.1	108.6	108.7
C(3)	— ^{e)}	41.6	42.5	C(4'b)	127.8	127.9	128.0
C(4)	61.1	61.3	61.4	C(5')	101.6	102.2	102.0
C(6)	52.0	52.4	52.6	C(6')	150.0	153.2	153.2
C(7)	28.7	28.9	28.9	C(7')	110.0	111.9	111.8
C(7a)	126.8	126.9	126.3	C(8')	110.9	111.4	111.4
C(8)	115.2	114.4	114.3	C(8'a)	129.9	130.6	130.3
C(9)	144.7 ^{f)}	146.9 ^{g)}	146.6 ^{j)}	C(9'a)	138.3	137.2 ^{h)}	137.2 ^{k)}
C(10)	145.7 ^{f)}	147.9 ^{g)}	147.8 ^{j)}	10-OMe	56.1	56.6	56.0
C(11)	109.6	109.7	108.8	9-OCH ₂ Ph	—	71.0	71.0
C(11a)	128.9	131.0	130.9	6'-OCH ₂ Ph	—	71.0	71.0
C(11b)	62.2	62.5	62.7	OCH ₂ Ph	—	137.7 ^{h)}	137.7 ^{k)}
C(12)	— ^{e)}	38.6	38.6 ⁱ⁾	—	—	137.5 ^{h)}	137.4 ^{k)}
C(13)	23.0	23.5	23.9	—	—	128.4	128.4
C(14)	11.0	11.1	11.3	—	—	127.6	127.6
C(1')	48.6	49.4	52.3	—	—	127.5	127.5
C(3')	41.5	42.0	42.9	—	—	127.2	127.2

a) In ppm downfield from internal Me₄Si. b) See formula (\pm)-**1** in Chart 1 for the numbering system. The carbon(s) indicated by underscoring in the partial structures is that to which the signal has been assigned. c) Measured in Me₂SO-*d*₆. d) Measured in CDCl₃. e) Overlapped with the signals of the solvent, Me₂SO-*d*₆. f–k) Assignments indicated by a given superscript may be interchanged.

TABLE II. ¹H-NMR Data for (\pm)-*O,O*-Dibenzyl-9-demethyltubulosine (**9**) and Its 1' α -H Isomer (\pm)-**12** in CDCl₃

Proton ^{a)}	Chemical shift (δ)		Proton ^{a)}	Chemical shift (δ)	
	(\pm)- 9	(\pm)- 12		(\pm)- 9	(\pm)- 12
CH ₂ Me	0.88 (t) ^{b)}	0.94 (t) ^{b)}	C(11)H	6.78 (s)	6.43 (s)
C(10)OMe	3.83 (s)	3.54 (s)	C(5')H	7.03 (d) ^{f)}	7.01 (d) ^{f)}
C(1')H	4.23 (d) ^{c)}	4.18 (t) ^{d)}	C(7')H	6.86 (dd) ^{g)}	6.85 (dd) ^{g)}
C(9)OCH ₂ Ph	5.10 (s)	5.06 (s) ^{e)}	C(8')H	7.19 (d) ^{h)}	7.19 (d) ^{h)}
C(6')OCH ₂ Ph	5.10 (s)	5.09 (s) ^{e)}	OCH ₂ Ph	7.2–7.5 (m)	7.2–7.5 (m)
C(8)H	6.60 (s)	6.55 (s)	N(9')H	7.81 (s)	7.86 (s)

a) See formula (\pm)-**1** in Chart 1 for the numbering system. The protons indicated by underscoring in the partial structures are those to which the signal has been assigned. b) With $J=6.6$ Hz. c) With $J=10.0$ Hz. d) Indistinct triplet with $J=5.0$ Hz. e) Assignments indicated by this superscript may be reversed. f) With $J=2.4$ Hz. g) With $J=8.8$ and 2.4 Hz. h) With $J=8.8$ Hz.

Popelak *et al.*¹³⁾ for isotubulosine (**19**) and tubulosine (**3**) and by us¹⁾ for **21** and alangimarckine (**17**). The shielding of the C(10)-methoxy protons in these and the present cases may be explained by assuming a preferred conformation (type **29**) of the 1'- α -H isomer in which the C(10)-methoxy group overhangs the indole moiety within the same molecule. This view is supported by the observation of an about 0.35-ppm upfield shift of the C(11)H proton signal of (\pm)-**12** or (\pm)-**11**, relative to that of (\pm)-**9** or (\pm)-**1**. It is of particular interest that the C(1')H proton signal of the 1'- β -H isomer (\pm)-**9** or (\pm)-**1** appeared as a doublet with $J = 10$ Hz, whereas that of the 1'- α -H isomer (\pm)-**12** or (\pm)-**11** appeared as a dull triplet with $J = 5.0$ or 5.5 Hz. We have observed that in CDCl₃ the C(1')H protons of the 1'- β -H isomers emetine (**26**) and alangimarckine (**17**) also resonate as a doublet ($J = 10.5$ Hz) at δ 4.16 and 4.27, respectively; those of the 1'- α -H isomers isoemetine (**27**) and **21** appear as a dull triplet ($J = 5.5$ Hz) at δ 4.10 and 4.22, respectively. The doublet pattern observed for the 1'- β -H isomers may be explained by assuming a C(1')-C(12) bond conformation close to that represented by the Newman projection formula **24**, whereas the triplet pattern of the 1'- α -H isomers may be a reflection of a **28**-type conformer. Thus, the coupling pattern of the C(1')H proton served as an additional diagnostic tool for the C(1') stereochemistry. On the basis of the above discussions on the ¹³C- and ¹H-NMR spectral data, we propose the preferred conformations **25** for the 1'- β -H isomers and **29** for the 1'- α -H isomers.

The synthetic sample of (\pm)-9-demethyltubulosine [(\pm)-**1**] described above was then compared directly with a natural sample⁴⁾ of (–)-demethyltubulosine isolated from *A. lamarckii*. Although the ultraviolet (UV) (in MeOH, 0.1 N aqueous NaOH, and 0.1 N aqueous HCl) and mass spectra of (\pm)-**1** were virtually identical with those of the natural sample, the ¹H-NMR spectra and TLC behavior of the two samples were not identical. Thus, the above results definitely exclude the structure **1** and indicate the alternative 10-demethyl structure (**2**) to be correct for the *A. lamarckii* alkaloid. This was subsequently confirmed by a racemic synthesis of **2** via a similar "lactim ether route";⁷⁾ the details will be published elsewhere shortly. On the other hand, it happened quite recently that our (\pm)-**1** was found to be identical, apart from the chiroptical properties and melting point, with a C₂₈H₃₅N₃O₃ alkaloid from *Alangium vitiense*.⁸⁾ Interestingly, the above synthesis of (\pm)-9-demethyltubulosine [(\pm)-**1**] thus turned out to have completed incidentally the racemic synthesis of the *A. vitiense* alkaloid demethyltubulosine instead of the *A. lamarckii* alkaloid demethyltubulosine, establishing the structure and relative stereochemistry of the former.

Experimental

General Notes—All melting points were determined with a Yamato MP-1 capillary melting point apparatus and are corrected. See ref. 10b for details of instrumentation and measurements. Microanalyses were performed by Mr. Y. Itatani and his associates at Kanazawa University. The following abbreviations are used: br=broad, d=doublet, dd=doublet-of-doublets, m=multiplet, q=quartet, s=singlet, sh=shoulder, t=triplet.

(\pm)-9-Benzoyloxy-N-[2-(5-benzoyloxy-1H-indol-3-yl)ethyl]-3 α -ethyl-1,3,4,6,7,11b α -hexahydro-10-methoxy-2H-benzo[a]quinolizine-2 β -acetamide [(\pm)-**8**]—Diethyl phosphorocyanidate¹⁵⁾ (587 mg, 3.6 mmol) and Et₃N (364 mg, 3.6 mmol) were successively added to a chilled, stirred solution of (\pm)-7·1/3EtOH¹⁰⁾ (765 mg, 1.8 mmol) and 5-benzoyloxytryptamine¹⁶⁾ (719 mg, 2.7 mmol) in HCONMe₂ (10 ml). The mixture was stirred at room temperature for 6 h and extracted with CHCl₃ after addition of H₂O (20 ml). The CHCl₃ extracts were washed with H₂O, dried over anhydrous Na₂SO₄, and concentrated *in vacuo* to leave an orange glass. The glass was crystallized from AcOEt and drying over P₂O₅ at 2 mmHg and room temperature for 20 h yielded an analytical sample, mp 92.5–94°C; IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm⁻¹: 3490 and 3460 (NH's), 2820 and 2760 (*trans*-quinolizidine ring),¹⁷⁾ 1730 (AcOEt), 1659 (amide CO); ¹H-NMR (CDCl₃) δ : 0.88 (3H, t, $J = 7$ Hz, CCH₂Me), 1.25 (1.5H, t, $J = 7$ Hz, AcOCH₂Me), 2.04 (1.5H, s, MeCO₂Et), 3.77 (3H, s, OMe), 4.12 (1H, q, $J = 7$ Hz, AcOCH₂Me), 5.09 (4H, s, two OCH₂Ph's), 5.57 (1H, t, $J = 5.5$ Hz, CONH), 6.61 (1H, s, H₍₈₎ or H₍₁₁₎), 6.70 (1H, s, H₍₁₁₎ or H₍₈₎), 6.91 (1H, dd, $J = 8.8$ and 2.4 Hz, H_{(6'})), 6.94 (1H, d, $J = 2.0$ Hz, H_(2')), 7.11 (1H, d, $J = 2.4$ Hz, H_(4')), 7.20 (1H, d, $J = 8.8$ Hz, H_(7')), 7.2–7.5 (10H, m, two OCH₂Ph's), 8.15 (1H, br, indole NH).¹⁸⁾ Anal. Calcd for C₄₂H₄₇N₃O₄·1/2CH₃CO₂C₂H₅: C, 75.29; H, 7.32; N, 5.99. Found: C, 75.54; H, 7.27; N, 6.20.

(\pm)-9-Benzyloxy-2 β -[(6-benzyloxy-4,9-dihydro-3H-pyrido[3,4-*b*]indol-1-yl)methyl]-3 α -ethyl-1,3,4,6,7,11 β -hexahydro-10-methoxy-2H-benzo[*a*]quinolizine [(\pm)-10]—A solution of (\pm)-8 \cdot 1/2AcOEt (1.12 g, 1.6 mmol) and POCl₃ (2.45 g, 16 mmol) in dry toluene (50 ml) was heated under reflux in an atmosphere of nitrogen for 2.5 h. The reaction mixture was concentrated *in vacuo*, and 5% aqueous KOH (40 ml) and CH₂Cl₂ (50 ml) were added to the oily residue under ice-cooling. The resulting mixture was stirred for 10 min, and the CH₂Cl₂ layer was separated from the aqueous layer, which was further extracted with CH₂Cl₂. The combined CH₂Cl₂ extracts were washed with saturated aqueous NaCl, dried over anhydrous Na₂SO₄, and evaporated *in vacuo* to leave a brown glass. The glass was chromatographed on a silica gel column [benzene–EtOH (10:1, v/v)] to give (\pm)-10 (704 mg, 69%) as a yellow glass, which crystallized from EtOH. Recrystallization from EtOH and drying over P₂O₅ at 2 mmHg and room temperature for 20 h furnished an analytical sample of (\pm)-10 \cdot 2H₂O \cdot EtOH as yellow minute needles, mp 105–106°C; IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 2770 (*trans*-quinolizidine ring);¹⁷ ¹H-NMR (CDCl₃) δ : 0.93 (3H, t, *J* = 7 Hz, CCH₂Me), 1.23 (3H, t, *J* = 7 Hz, MeCH₂OH), 1.98 (H₂O), 3.51 (3H, s, OMe), 3.70 (2H, q, *J* = 7 Hz, MeCH₂OH), 5.04 and 5.10 (2H each, s, two OCH₂Ph's), 6.40 (1H, s, H₍₈₎ or H₍₁₁₎), 6.55 (1H, s, H₍₁₁₎ or H₍₈₎), 6.9–7.5 (13H, m, H₍₅₎, H₍₇₎, H₍₈₎); and two OCH₂Ph's), 8.46 (1H, br, NH). *Anal.* Calcd for C₄₂H₄₅N₃O₃ \cdot 2H₂O \cdot C₂H₅OH: C, 73.20; H, 7.68; N, 5.82. Found: C, 73.19; H, 7.48; N, 5.96.

[2R*-[2 α (S*),3 β ,11 β]]- and [2R*-[2 α (R*),3 β ,11 β]]-9-Benzyloxy-2-[(6-benzyloxy-2,3,4,9-tetrahydro-1H-pyrido[3,4-*b*]indol-1-yl)methyl]-3-ethyl-1,3,4,6,7,11 β -hexahydro-10-methoxy-2H-benzo[*a*]quinolizines [(\pm)-9 and (\pm)-12]—A solution of (\pm)-10 \cdot 2H₂O \cdot EtOH (541 mg, 0.75 mmol) in dioxane (10 ml) was hydrogenated over Adams catalyst (80 mg) at atmospheric pressure and 29°C for 40 min. Removal of the catalyst by filtration and evaporation of the filtrate under reduced pressure left a yellowish oil, which was dissolved in CHCl₃ (60 ml). The CHCl₃ solution was washed successively with 5% aqueous NaOH and saturated aqueous NaCl, dried over anhydrous Na₂SO₄, and concentrated *in vacuo* to leave a brown glass (470 mg). This material was then chromatographed on a silica gel column using CHCl₃–EtOH (10:1, v/v) as eluent. Earlier fractions afforded (\pm)-O,*O*-dibenzyl-9-demethyltubulosine [(\pm)-9] (140 mg, 29%) as a pale yellowish glass, TLC *R*_f 0.59 or 0.45 [silica gel, CHCl₃–EtOH (10:1, v/v) or benzene–EtOH (10:1, v/v)]; MS *m/e*: 641 (M⁺); IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm⁻¹: 3490 (indole NH), 3390 [N(2')H], 2820 and 2760 (*trans*-quinolizidine ring);¹⁷ ¹H-NMR (Table II); ¹³C-NMR (Table I).

Later fractions in the above chromatography furnished the 1' α -H isomer (\pm)-12 (262 mg, 54%) as a pale yellowish glass, TLC *R*_f 0.50 or 0.40 [silica gel, CHCl₃–EtOH (10:1, v/v) or benzene–EtOH (10:1, v/v)]; MS *m/e*: 641 (M⁺); IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm⁻¹: 3490 (indole NH), 3390 [N(2')H], 2820 and 2760 (*trans*-quinolizidine ring);¹⁷ ¹H-NMR (Table II); ¹³C-NMR (Table I).

[2R*-[2 α (S*),3 β ,11 β]]-3-Ethyl-1,3,4,6,7,11 β -hexahydro-9-hydroxy-2-[(6-hydroxy-2,3,4,9-tetrahydro-1H-pyrido[3,4-*b*]indol-1-yl)methyl]-10-methoxy-2H-benzo[*a*]quinolizine [(\pm)-9-Demethyltubulosine] [(\pm)-1]—A solution of (\pm)-9 (120 mg, 0.19 mmol) in MeOH–AcOH (1:1, v/v) (10 ml) was hydrogenated over 10% Pd–C (120 mg) at atmospheric pressure and 27°C for 3 h. The catalyst was removed by filtration and washed with MeOH (20 ml). The filtrate and washings were combined and concentrated *in vacuo*, and H₂O (3 ml) was added to the oily residue. The aqueous mixture was filtered and the filtrate was alkalinized with 10% aqueous Na₂CO₃. The precipitate that resulted was filtered off, washed with H₂O, and dried to give (\pm)-1 \cdot 2H₂O (75 mg, 81%) as a pale yellowish solid, mp 212–214°C (dec.). Recrystallization from MeOH–CH₂Cl₂ (1:3, v/v) and drying over P₂O₅ at 2 mmHg and room temperature for 20 h produced an analytical sample as colorless minute needles, mp 213–214°C (dec.); TLC *R*_f 0.39 [silica gel, CHCl₃–MeOH (2:1, v/v)]; MS *m/e* (relative intensity): 462 (M⁺ + 1) (21), 461 (M⁺) (75), 272 (20), 271 (22), 261 (28), 260 (30), 259 (31), 258 (86), 256 (36), 232 (51), 230 (41), 201 (59), 200 (39), 199 (44), 191 (39), 187 (100), 178 (42), 177 (31); UV λ_{max} (MeOH) 281.5 nm (ϵ 12800); λ_{max} (0.1 N aqueous NaOH) 282 (10800), 304 (sh) (8020), 326 (sh) (3940); λ_{max} (0.1 N aqueous HCl) 276.5 (11500); ¹H-NMR (Me₂SO-*d*₆) δ : 3.71 (3H, s, OMe), 4.15 (1H, d, *J* = 10 Hz, H₍₁₎), 6.47 (1H, s, H₍₈₎), 6.49 (1H, dd, *J* = 8.7 and 2.0 Hz, H₍₇₎), 6.66 (1H, d, *J* = 2.0 Hz, H₍₅₎), 6.78 (1H, s, H₍₁₁₎), 7.03 (1H, d, *J* = 8.7 Hz, H₍₈₎), 8.45, 8.68, and 10.25 (br, NH's and OH's); ¹³C-NMR (Table I). *Anal.* Calcd for C₂₈H₃₅N₃O₃ \cdot 2H₂O: C, 67.58; H, 7.90; N, 8.44. Found: C, 67.59; H, 7.68; N, 8.44. The spectral data and TLC mobility were identical with those of the C₂₈H₃₅N₃O₃ alkaloid [mp 200°C; $[\alpha]_{\text{D}}^{20}$ –40° (*c* = 1, pyridine)] isolated from *Alangium vitiense*.⁸⁾ On the other hand, the ¹H-NMR spectrum and TLC behavior of this (\pm)-1 were not identical with those of (–)-demethyltubulosine⁴⁾ isolated from *A. lamarckii*.

[2R*-[2 α (R*),3 β ,11 β]]-3-Ethyl-1,3,4,6,7,11 β -hexahydro-9-hydroxy-2-[(6-hydroxy-2,3,4,9-tetrahydro-1H-pyrido[3,4-*b*]indol-1-yl)methyl]-10-methoxy-2H-benzo[*a*]quinolizine [(\pm)-11]—Debenzylation of (\pm)-12 and work-up of the reaction mixture were carried out as described above for (\pm)-1, producing (\pm)-11 (86% yield) as a yellowish solid. Recrystallization of the solid from EtOH provided an analytical sample as colorless prisms, mp 235–236.5°C (dec.); TLC *R*_f 0.27 [silica gel, CHCl₃–MeOH (2:1, v/v)]; MS *m/e*: 461 (M⁺); UV λ_{max} (MeOH) 281.5 nm (ϵ 11900); λ_{max} (0.1 N aqueous NaOH) 282 (10300), 304 (sh) (7720), 326 (sh) (4300); λ_{max} (0.1 N aqueous HCl) 276.5 (10700); ¹H-NMR (Me₂SO-*d*₆) δ : 3.49 (3H, s, OMe), 4.18 (1H, dull t, *J* = 5.5 Hz, H₍₁₎), 6.41 (1H, s, H₍₈₎ or H₍₁₁₎), 6.44 (1H, s, H₍₁₁₎ or H₍₈₎), 6.51 (1H, dd, *J* = 8.5 and 2.0 Hz, H₍₇₎), 6.67 (1H, d, *J* = 2.0 Hz, H₍₅₎), 7.07 (1H, d, *J* = 8.5 Hz, H₍₈₎), 8.50, 8.61, and 10.41 (br, NH's and OH's). *Anal.* Calcd for C₂₈H₃₅N₃O₃: C, 72.86; H, 7.64; N, 9.10. Found: C, 73.00; H, 7.62; N, 8.93.

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